Abstract 4567: A prospective exploratory clinical study of penpulimab plus anlotinib as first-line treatment for locally advanced or metastatic urothelial carcinoma

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Background:

- Immune checkpoint inhibitors have been implemented in the management of cisplatin-ineligible locally advanced or metastatic urothelial carcinoma (la/mUC)[1-2].
- Penpulimab is a programmed death 1 (PD-1) inhibitor which was approved by the Chinese National Medical Products Administration (NMPA) in August 2021. Anlotinib is a novel oral multi-target tyrosine kinase inhibitor targeting VEGFR, FGFR, PDGFR and c-Kit.
- This single-arm, phase Ⅱ, prospective clinical trial (ChiCTR1900028022) aimed to assess the efficacy and safety of penpulimab plus anlotinib as first-line therapy for la/mUC.

Methods:

Eligibility Criteria (N=30)
- 18-75 years old
- Advanced/metastatic urothelial carcinoma;
- No prior systematic treatment
- ECOG PS of 0-2
- ≧ 1 Measurable lesions according to RECIST v1.1

Penpulimab
200mg IV Q3W
+
Anlotinib
8 mg orally QD D1-14
every 3 weeks

Primary endpoint
- ORR

Secondary endpoints
- DCR
- PFS
- Safety

Results

- As of May 2022, 12 patients (pts) were enrolled and received treatment. Ten pts accepted treatment and were evaluable. (Figure 2), which inferred the ORR of 60% (95%CI, 26.2%-87.8%) and the DCR of 90% (95%CI, 55.5%-99.7%) (Table 1). The median age was 66 (range, 53-74) and 100% (10/10) of patients had metastatic lesions. Baseline characteristics was shown in Table 2.
- The median PFS was 12.1 (95%CI, 4.1-20.1) months (Figure 1). The median time to the first response was 1.6 (95%CI, 1.3-1.8) months (Figure 3) .

Safety

- Treatment-emergent adverse event (TEAE) were reported in 90% of pts, and Grade ≥3 TEAEs were reported in 10% patients (Table 3).

Conclusions : First-line penpulimab in combination with anlotinib in patients with locally advanced or metastatic urothelial carcinoma showed promising efficacy and manageable safety.

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Table 1. Objective tumor response (according to RECIST v1.1)

Best response (N=10)	n (%)
Complete response	2 (20)
Partial response	4 (40)
Stable disease	3 (30)
Progressive disease	1 (10)
ORR % (95% CI)	60% (26.2-87.8)
DCR % (95% CI)	90% (55.5-99.7)

Figure 1. Progression-free survival (n =10)

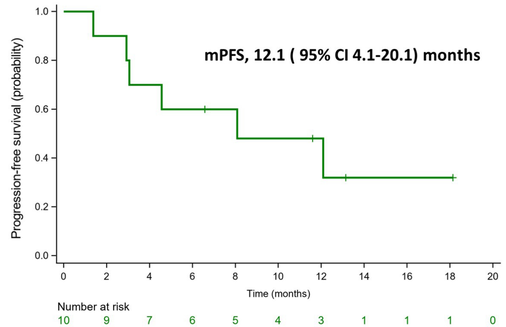

Figure 2. Percent best change in target lesion size form baseline (n =10)

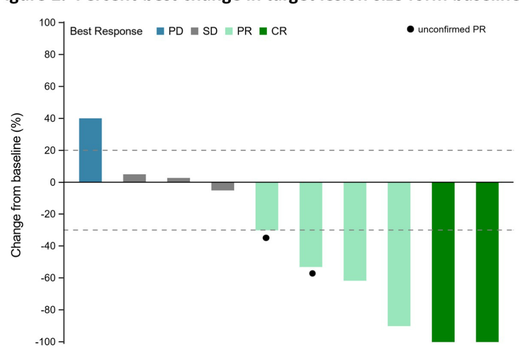

Figure 3. Median time to response (n =10)

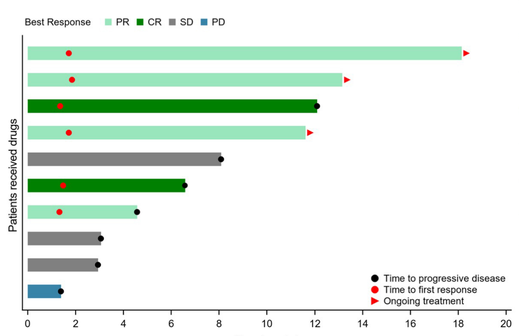

Table 2. Baseline characteristics

Characteristic (N=10)	n (%)
Median age, years (range)	66 (53-74)
Male, n (%)	9 (90%)
ECOG PS, n (%)	
0 1	2 (20%) 8 (80%)
Cancer type, n (%)	
Bladder Renal pelvis Ureter	5 (50%) 3 (30%) 2 (20%)
Metastatic disease site, n(%)	
Lymph nodes Visceral disease Bone	7 (70%) 3 (30%) 3 (30%)

Table 3. Treatment-emergent adverse events

Adverse events	Penplimab + Anlotinib, n (%)		
	All grade	Grade 1 or 2	Grade 3 or 4
Hyperthyroidism	2 (20)	2 (20)	0
Creatinine increased	2 (20)	2 (20)	0
Haematuria	2 (20)	2 (20)	0
Hypertension	1 (10)	1 (10)	0
INR incerased	1 (10)	1 (10)	0
Liver dysfunction	1 (10)	0	1 (10)
ALT increased	1 (10)	1 (10)	0
Anaemia	1 (10)	1 (10)	0
Rash	1 (10)	1 (10)	0
Leucocyte decreased	1 (10)	1 (10)	0
Renal dysfunction	1 (10)	1 (10)	0
Platelet count decreased	1 (10)	1 (10)	0
Fatigue	1 (10)	1 (10)	0
Weight decreased	1 (10)	1 (10)	0

References [1] Vuky J, Balar A V, Castellano D, et al. Long-term outcomes in KEYNOTE-052[J]. Journal of Clinical Oncology, 2020, 38(23): 2658-2666.[2] Pal S K,Frankel P H, Mortazavi A,et al. Effect of cisplatin and gemcitabine with or without berzosertib in patients with advanced urothelial carcinoma[J]. JAMA oncology, 2021, 7(10): 1536-1543.